

**Amendment and Response**

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Serial No.: 10/027,226

Confirmation No.: 9039

Filed: 20 December 2001

**For: METHODS AND DEVICES FOR REMOVAL OF ORGANIC MOLECULES FROM BIOLOGICAL MIXTURES USING A HYDROPHILIC SOLID SUPPORT IN A HYDROPHOBIC MATRIX**

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**Amendments to the Claims**

This listing of claims replaces all prior versions, and listings, of claims in the above-identified application:

1. **(Withdrawn - Currently Amended)** A method of removing small negatively charged organic molecules from a biological sample mixture, the method comprising:
  - providing a device comprising a plurality of process arrays, wherein each process array of the plurality of process arrays comprises:
    - a plurality of process chambers, each of the process chambers defining a volume for containing a biological sample mixture; and
    - at least one distribution channel connecting the plurality of process chambers of the array; wherein at least one of the process arrays comprises, within the array, a solid-phase extraction material comprising particles of a hydrophilic solid support at least partially embedded within a hydrophobic matrix;
  - providing a biological sample mixture; and
  - contacting the biological sample mixture with the solid-phase extraction material to remove at least a portion of the small negatively charged organic molecules from the biological sample mixture.
2. **(Canceled)**
3. **(Withdrawn)** The method of claim 1 wherein the particles have an average particle size of at least about 5 nm.
4. **(Withdrawn)** The method of claim 3 wherein the particles have an average particle size of no greater than about 500 microns.

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5. **(Withdrawn)** The method of claim 1 wherein the particles of hydrophilic solid support comprise a material selected from the group consisting of inorganic particles, naturally occurring organic polymeric materials, synthetic or modified naturally occurring organic polymers, vitreous materials, plastics that are intrinsically hydrophilic or modified to be hydrophilic by the presence of hydrophilic functional groups, and mixtures thereof.
6. **(Withdrawn)** The method of claim 1 wherein the hydrophobic matrix comprises a polymeric material selected from the group consisting of a silicone, polyvinyl butyral, polyolefin, natural or synthetic rubber, fluorinated polymer, acrylate, epoxy, and combinations thereof.
7. **(Withdrawn)** The method of claim 6 wherein the hydrophobic matrix comprises an adhesive.
8. **(Withdrawn)** The method of claim 7 wherein the adhesive is a pressure sensitive adhesive.
9. **(Withdrawn)** The method of claim 1 wherein the biological sample mixture is a nucleic acid sequencing reaction mixture.
10. **(Withdrawn)** The method of claim 9 wherein the small negatively charged organic molecules are selected from the group consisting of dye-labeled terminators, primers, degraded dye molecules, deoxynucleotide triphosphates, and mixtures thereof.
11. **(Withdrawn)** The method of claim 10 wherein the small negatively charged organic molecules comprise dye-labeled terminators.

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12. **(Withdrawn)** The method of claim 11 wherein the dye-labeled terminators are selected from the group consisting of dideoxynucleotide triphosphates, dideoxynucleotide diphosphates, dideoxynucleotide monophosphates, dideoxynucleosides, and combinations thereof.
13. **(Withdrawn)** The method of claim 10 wherein contacting the biological sample mixture with the solid-phase extraction material is carried out under conditions effective to remove substantially all the dye-labeled terminators from the biological sample mixture.
14. **(Withdrawn)** The method of claim 1 wherein the biological sample mixture is a PCR reaction mixture.
15. **(Withdrawn)** The method of claim 14 wherein the small negatively charged organic molecules are selected from the group consisting of primers, degraded dye molecules, deoxynucleotide triphosphates, and mixtures thereof.
16. **(Withdrawn)** The method of claim 15 wherein contacting the biological sample mixture with the solid-phase extraction material is carried out under conditions effective to remove substantially all the primers from the biological sample mixture.
17. **(Withdrawn)** The method of claim 1 wherein the small negatively charged organic molecules have a molecular weight of less than about 6,000.
18. **(Withdrawn)** The method of claim 1 wherein the device is a microfluidic device.
19. **(Withdrawn)** The method of claim 1 wherein contacting the biological sample mixture

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with the solid-phase extraction material comprises agitating while contacting.

20. **(Withdrawn - Currently Amended)** A method of removing small negatively charged organic molecules from a biological sample mixture, the method comprising:

providing a device comprising a plurality of process arrays, wherein each process array of the plurality of process arrays comprises:

a plurality of process chambers, each of the process chambers defining a volume for containing a biological sample mixture; and

at least one distribution channel connecting the plurality of process chambers of the array; wherein at least one of the process arrays comprises, within the array, a solid-phase extraction material comprising hydrophilic particles disposed on a layer of a hydrophobic matrix and at least partially embedded therein;

providing a biological sample mixture; and

contacting the biological sample mixture with the solid-phase extraction material to remove at least a portion of the small negatively charged organic molecules from the biological sample mixture.

21. **(Withdrawn)** The method of claim 20 wherein the particles are disposed on the layer of hydrophobic matrix at a density of about 0.1 mg per 12 mm<sup>2</sup> surface area to about 5 mg per 12 mm<sup>2</sup> surface area.

22. **(Withdrawn)** The method of claim 20 wherein the layer of hydrophobic material comprises a layer of an adhesive.

23. **(Withdrawn)** The method of claim 22 wherein the layer of an adhesive comprises a layer of a pressure sensitive adhesive.

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24. **(Withdrawn)** The method of claim 20 wherein the device is a microfluidic device.
25. **(Withdrawn)** The method of claim 20 wherein contacting the biological sample mixture with the solid-phase extraction material comprises agitating while contacting.
26. **(Withdrawn - Currently Amended)** A method of removing small negatively charged organic molecules from a biological sample mixture, the method comprising:
- providing a device comprising a plurality of process arrays, wherein each process array of the plurality of process arrays comprises:
    - a plurality of process chambers, each of the process chambers defining a volume for containing a biological sample mixture; and
    - at least one distribution channel connecting the plurality of process chambers of the array; wherein at least one of the process arrays comprises, within the array, a solid-phase extraction material comprising particles of a hydrophilic solid support at least partially embedded within a hydrophobic matrix;
  - providing a biological sample mixture; and
  - contacting the biological sample mixture with the solid-phase extraction material to remove at least a portion of the small negatively charged organic molecules from the biological sample mixture;
  - wherein the biological sample mixture comprises a nucleic acid amplification reaction mixture.
27. **(Withdrawn)** The method of claim 26 wherein the device is a microfluidic device.
28. **(Withdrawn - Currently Amended)** A method of removing small negatively charged organic molecules from a biological sample mixture, the method comprising:

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providing a device comprising a plurality of process arrays, wherein each process array of the plurality of process arrays comprises:

a plurality of process chambers, each of the process chambers defining a volume for containing a biological sample mixture; and

at least one distribution channel connecting the plurality of process chambers of the array; wherein at least one of the process arrays comprises, within the array, a solid-phase extraction material, wherein the solid-phase extraction material comprises particles of a hydrophilic solid support at least partially embedded within a hydrophobic matrix;

providing a biological sample mixture in the at least one process array; and

transferring the biological sample mixture within the at least one process array, wherein the biological sample mixture and the solid-phase extraction material remain in contact for a sufficient time to remove at least a portion of the small negatively charged organic molecules from the biological sample mixture.

29. **(Canceled)**

30. **(Withdrawn)** The method of claim 28 wherein the particles have an average particle size of at least about 5 nm.

31. **(Withdrawn)** The method of claim 30 wherein the particles have an average particle size of no greater than about 500 microns.

32. **(Withdrawn)** The method of claim 28 wherein the particles of hydrophilic solid support comprise a material selected from the group consisting of inorganic particles, naturally occurring organic polymeric materials, synthetic or modified naturally occurring organic polymers, vitreous materials, plastics that are intrinsically hydrophilic or modified to be hydrophilic by the presence

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of hydrophilic functional groups, and mixtures thereof.

33. **(Withdrawn)** The method of claim 28 wherein the hydrophobic matrix comprises a polymeric material selected from the group consisting of a silicone, polyvinyl butyral, polyolefin, natural or synthetic rubber, fluorinated polymer, acrylate, epoxy, and combinations thereof.
34. **(Withdrawn)** The method of claim 28 wherein the hydrophobic matrix comprises an adhesive.
35. **(Withdrawn)** The method of claim 34 wherein the adhesive is a pressure sensitive adhesive.
36. **(Withdrawn)** The method of claim 28 wherein the biological sample mixture is a nucleic acid sequencing reaction mixture.
37. **(Withdrawn)** The method of claim 36 wherein the small negatively charged organic molecules are selected from the group consisting of dye-labeled terminators, primers, degraded dye molecules, deoxynucleotide triphosphates, and mixtures thereof.
38. **(Withdrawn)** The method of claim 36 wherein the small negatively charged organic molecules comprise dye-labeled terminators.
39. **(Withdrawn)** The method of claim 38 wherein the dye-labeled terminators are selected from the group consisting of dideoxynucleotide triphosphates, dideoxynucleotide diphosphates, dideoxynucleotide monophosphates, dideoxynucleosides, and combinations thereof.

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40. **(Withdrawn)** The method of claim 38 wherein the biological sample mixture with the solid-phase extraction material are contacted under conditions effective to remove substantially all the dye-labeled terminators from the biological sample mixture.
41. **(Withdrawn)** The method of claim 28 wherein the biological sample mixture is a PCR reaction mixture.
42. **(Withdrawn)** The method of claim 41 wherein the small negatively charged organic molecules are selected from the group consisting of primers, degraded dye molecules, deoxynucleotide triphosphates, and mixtures thereof.
43. **(Withdrawn)** The method of claim 42 wherein the biological sample mixture and the solid-phase extraction material are contacted under conditions effective to remove substantially all the primers from the biological sample mixture.
44. **(Withdrawn)** The method of claim 28 wherein the small negatively charged organic molecules have a molecular weight of less than about 6,000.
45. **(Withdrawn)** The method of claim 28 wherein the biological sample mixture and the solid-phase extraction material are agitated while in contact.
46. **(Withdrawn)** The method of claim 28 wherein the at least one process array comprises a loading chamber and at least one process chamber.
47. **(Withdrawn - Currently Amended)** A method of removing small negatively charged organic molecules from a biological sample mixture, the method comprising:



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providing a device comprising a plurality of process arrays, wherein each process array of the plurality of process arrays comprises:

a plurality of process chambers, each of the process chambers defining a volume for containing a biological sample mixture; and

at least one distribution channel connecting the plurality of process chambers of the array; wherein at least one of the process arrays comprises, within the array, a solid-phase extraction material, wherein the solid-phase extraction material comprises hydrophilic particles disposed on a layer of a hydrophobic matrix and at least partially embedded therein;

providing a biological sample mixture in the at least one process array; and

transferring the biological sample mixture within the at least one process array, wherein the biological sample mixture and the solid-phase extraction material remain in contact for a sufficient time to remove at least a portion of the small negatively charged organic molecules from the biological sample mixture.

48. **(Withdrawn)** The method of claim 47 wherein the biological sample mixture comprises a nucleic acid amplification reaction mixture.

49. **(Withdrawn)** The method of claim 47 wherein the biological sample mixture and the solid-phase extraction material are agitated while in contact.

50. **(Currently Amended)** A device comprising:

a plurality of process arrays, wherein each process array of the plurality of process arrays comprises:

a plurality of process chambers, each of the process chambers defining a volume for containing a biological sample mixture; and

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at least one distribution channel connecting the plurality of process chambers of the array;

wherein at least one of the process arrays comprises a solid-phase extraction material within the array;

wherein the solid-phase extraction material comprises particles of a hydrophilic solid support at least partially embedded within a hydrophobic matrix; and

wherein the device is operable to remove small negatively charged organic molecules from the biological sample mixture.

51. **(Original)** The device of claim 50 further comprising a plurality of valves, wherein at least one of the valves is located along the at least one distribution channel.

52. **(Original)** The device of claim 50 wherein the plurality of process arrays comprises a plurality of independent process arrays.

53. **(Original)** The device of claim 50 wherein the plurality of process arrays are arranged radially on the device.

54. **(Original)** The device of claim 50 wherein the hydrophobic matrix comprises an adhesive.

55. **(Previously Presented)** The device of claim 54 wherein the particles of hydrophilic solid support are pattern coated on a layer of the hydrophobic matrix.

56-61. **(Canceled)**

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62. **(Previously Presented)** The device of claim 50 wherein the particles of hydrophilic solid support have an average particle size of at least about 5 nm.

63. **(Previously Presented)** The device of claim 50 wherein the particles of hydrophilic solid support have an average particle size of no greater than about 500 microns.

64. **(Previously Presented)** The device of claim 50 wherein the particles of hydrophilic solid support comprise a material selected from the group consisting of inorganic particles, naturally occurring organic polymeric materials, synthetic or modified naturally occurring organic polymers, vitreous materials, plastics that are intrinsically hydrophilic or modified to be hydrophilic by the presence of hydrophilic functional groups, and mixtures thereof.

65. **(Previously Presented)** The device of claim 50 wherein the hydrophobic matrix comprises a polymeric material selected from the group consisting of a silicone, polyvinyl butyral, polyolefin, natural or synthetic rubber, fluorinated polymer, acrylate, epoxy, and combinations thereof.

66. **(Previously Presented)** The device of claim 50 wherein the hydrophobic matrix comprises an adhesive.

67. **(Previously Presented)** The device of claim 66 wherein the adhesive is a pressure sensitive adhesive.

68-76. **(Canceled)**

77. **(Previously Presented)** The device of claim 50 wherein the device is a microfluidic

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device.

78. (Currently Amended) A device comprising:

a plurality of process arrays, wherein each process array of the plurality of process arrays comprises:

a plurality of process chambers, each of the process chambers defining a volume for containing a biological sample mixture; and

at least one distribution channel connecting the plurality of process chambers of the array;

wherein at least one of the process arrays comprises a solid-phase extraction material within the array;

wherein the solid-phase extraction material comprises hydrophilic particles disposed on a layer of a hydrophobic matrix and at least partially embedded therein; and

wherein the device is operable to remove small negatively charged organic molecules from the biological sample mixture.